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IN THE

Supreme Court of the United States

MYLAN INC., et al,

Petitioners,

v.

DAIICHI SANKYO COMPANY LTD.
AND DAIICHI SANKYO, INC.,

Respondents.

ON PETITION FOR WRIT OF CERTIORARI TO THE
UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

BRIEF *AMICUS CURIAE* OF GENERIC PHARMACEUTICAL ASSOCIATION IN SUPPORT OF PETITIONERS

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Schering-Plough Corp. v. FTC, 402 F.3d 1056 (11th Cir. 2005) 6

Cited Authorities

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Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd., 492 F.3d 1350 (Fed. Cir. 2007) 4, 13, 15

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U.S. CONST., art. I, § 8, cl. 8 ..... 2, 5

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OTHER AUTHORITIES

149 Cong. Rec. H7531 (2003) 9

Matthew Avery, *Continuing Abuse of the Hatch-Waxman Act by Pharmaceutical Patent Holders & the Failure of the 2003 Amendments*, 60 Hastings L.J. 171 (2008) 8

Vincent L. Capuano, *Obviousness of Chemical Compounds: the "Lead Compound" Concept*, Intellectual Property Today 33 (July 2007) 14, 16

Cited Authorities

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Ceci Connolly & Kendra Marr, *As Budgets Tighten, More People Decide Medical Care Can Wait*, Wash. Post, Oct. 16, 2008 9

Rebecca S. Eisenberg, *Pharma's Nonobvious Problem*, 12 Lewis & Clark L. Rev. 375 (2008) 15

Expanding the Use of Generic Drugs, APSE Issue Brief, U.S. Dep't of Health & Human Servs. (Dec. 1, 2010) 7, 8, 10

M. L. Hayes, *Three Years Post-KSR: A Practitioner's Guide to 'Winning' Arguments on Obviousness and a Look at What May Lay Ahead*, 9 Nw. J. Tech. & Intell. Prop. 243 (2010) 14

Scott D. Locke, *Protecting Pharmaceutical Inventions in a KSR World*, 50 IDEA 1 (2009) 13

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Potential Federal & State-by-State Savings if Medicaid Pharmacy Programs were Optimally Managed, The Lewin Group (Dec. 2010)..... 10

Cited Authorities

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Robert H. Resis, *Lessons to Learn: From Post-KSR Pharmaceutical Obviousness Decisions*, 2 Landslide 40 (2009) 14

Savings Achieved Through the Use of Generic Pharmaceuticals, 2000-2009 (July 2010) 7, 9, 10

Margus Viigimaa, *ESH Hypertension Excellence Centres: A New Strategy to Combat an Old Foe*, J. Hypertension (2007) 8

INTEREST OF AMICUS CURIAE[1]

Amicus curiae the Generic Pharmaceutical Association ("GPhA") is a non-profit, voluntary association comprised of more than 80 manufacturers and distributors in the generic pharmaceutical industry, which in turn accounts for over 75 percent of prescriptions dispensed in the United States each year. GPhA's members provide American consumers with safe and cost-effective medicines that are bioequivalent to, and have the same safety, efficacy, and therapeutic benefit as, their brand-name counterparts. These products significantly improve public health while cutting annual healthcare costs by billions of dollars.

GPhA's core purpose is to improve the lives of consumers by providing timely access to affordable pharmaceuticals. Toward this end, GPhA advances the interests of its members through initiatives in the scientific, regulatory, federal and state forums and in the public affairs arena. GPhA also regularly participates as amicus curiae in cases before the Federal Circuit and the Supreme Court.

GPhA fully endorses the petition for certiorari filed by Petitioners and the reasons stated therein for granting certiorari. GPhA writes separately to emphasize the importance of this case in terms of its significant effect on the massive national market for prescription drugs and to explain why the "lead compound" test employed

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1. No counsel for a party authored this brief in whole or in part, and no such counsel or party made a monetary contribution intended to fund the preparation or submission of this brief. No person other than the amicus curiae, or its counsel, made a monetary contribution to its preparation or submission. The parties have been given notice of amicus curiae's intention to file this brief and have consented thereto.

by the Federal Circuit for adjudging the obviousness requirement for patentability is irreconcilable with this Court's decision in *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398 (2007).

REASONS FOR GRANTING THE PETITION

This case presents an important question concerning the proper standard under the federal patent laws for determining obviousness of advancements made in the field of medicinal chemistry. Specifically, the Petition presents the question whether the Federal Circuit's utilization of its rigid "lead compound" test as the sole means for determining obviousness of a chemical compound conflicts with this Court's admonition in *KSR* that obviousness demands a broad, common-sense inquiry. *Id.* at 419.

The importance of this federal question is indisputable—a threshold for nonobviousness that is too low will afford patent protection to advancements in pharmaceutical drug development that are unworthy of such protection. This will devalue prior inventions and skew the incentives for innovation, thus retarding "the Progress of Science and useful Arts," U.S. CONST., art. I, § 8, cl. 8, and impeding the important federal objective of bringing generic drugs to market faster, *see* Hatch-Waxman Act, 21 U.S.C. § 355 (the "Act"); *see also* H.R. Rep. No. 98-857, pt. 1, at 14 (1984) (noting that the purpose of the act is "to make available more low cost generic drugs").

More practically, conferring patent monopolies on "obvious" advancements will significantly delay market

entry of generic pharmaceutical drugs, which will lessen competition and harm the public in multiple respects. The availability of generics saves the nation's health care system a staggering amount of money. In 2009 alone, the use of generics instead of brand-name prescriptions saved the national health care system over $140 billion dollars—that is, *more than $1 billion dollars every three days.* When brand-name and generic drug manufacturers do not compete, prescription drug prices soar and consumers suffer. Indeed, the availability of generic alternatives could save a person who takes only a few prescription drugs hundreds, if not thousands, of dollars per year. This financial harm will only increase with the rising costs of brand-name prescription drugs, especially given that the cost of generic prescription drugs is decreasing. Worse still, high prices for brand-name prescription drugs often cause those afflicted to skip needed doses or forgo obtaining expensive prescription drugs altogether.

In addition, because the federal government is the largest purchaser of pharmaceutical drugs, delaying generic drugs from entering the market will cause serious harm to the public fisc and thus to American taxpayers. Approximately 68% of prescriptions purchased through Medicaid FFS (fee-for-service) are generics, but Medicaid would save an additional $1 billion annually for every 2% increase in generic utilization.

The Federal Circuit's rigid "lead compound" test is significantly contributing to this problem. This test sets far too low a threshold for nonobviousness. Indeed, since the enactment of the Hatch-Waxman Act in 1984, the Federal Circuit has *never found a single chemical compound claim to be obvious*, thus delaying market

entry of every generic drug at issue in this line of cases and eviscerating the pro-competitive purpose of the Act.

The Federal Circuit's "lead compound" test—and thus the decision below—conflicts with *KSR* in at least two important respects. *First*, adjudging obviousness under a test with a single determinant is fundamentally incompatible with the *KSR* Court's instruction that courts employ a "broad inquiry" that "take[s] account of the inferences and creative steps that a person of ordinary skill in the art would employ." 550 U.S. at 418.

Second, the "lead compound" test is flawed under *KSR* because it focuses on the motivation to select a particular lead compound from the prior art and to modify that compound in such a way as to arrive at the patented compound. *See Daiichi Sankyo Co., Ltd. v. Matrix Labs, Ltd.*, 619 F.3d 1346, 1352 (Fed. Cir. 2010); *see also Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007) (noting that even after *KSR* "it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness of a new claimed compound"). This narrow focus on particular motivations regarding only one (or even a few) so-called lead compounds is impossible to square with the Court's restoration of the common-sense "obvious to try" inquiry that the Federal Circuit had rejected in *KSR*, 550 U.S. at 421, and with common practice in the field of medicinal chemistry, which involves constant and routine optimization of known compounds in an iterative process of trial and error.

In short, the Federal Circuit in this case "has decided an important federal question in a way that conflicts

with relevant decisions of this Court." S. Ct. Rule 10(c). Moreover, this case is an ideal vehicle for resolving the question presented. *See* Pet. at 29-31.[2] There is only one claim of one patent at issue, and Petitioner stipulated that it infringed the patent, asserting obviousness as its only defense. In other words, the only contested issue in the case is the obviousness of one patent claim. A grant of certiorari thus is warranted and appropriate.

I. THE PETITION SATISFIES THE RULE 10(c) STANDARD FOR GRANTING CERTIORARI.

A. The Petition Presents A Federal Question Of Great Importance.

The question presented by the petition for certiorari addresses the proper standard for determining obviousness in the context of chemical compounds. This is an issue of great national importance because it bears directly upon the patentability of advancements in the field of medicinal chemistry. Enforcing the obviousness requirement for patentability is essential to "promot[ing] the Progress of Science and useful Arts." U.S. CONST., art. I, § 8, cl. 8. The nonobviousness requirement for patentability reflects the fact that an essential component of the *quid pro quo* for the limited monopoly conferred upon a patentee is "substantial creative effort." *Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 161 (1989). Indeed, "[g]ranting patent protection to advances that would occur in the ordinary course without real innovation retards progress . . . ." *KSR*, 550 U.S. at 419. It "deprive[s] prior inventions of their value or utility," *id.*, and confers monopoly rights

2. References to "Pet." are to the Petition. References to "Pet. App." are to the Petition's Appendix.

on minor advancements unworthy of such protection. Such a result would contradict the intentions of the Framers, whose "abhorrence of monopoly" drove them to ensure that the patent protection would not be granted for "small details [or] obvious improvements." *Graham v. John Deere Co.*, 383 U.S. 1, 7-9 (1966) (discussing the writings of Thomas Jefferson, the "first administrator of our patent system [and] the author of the 1793 Patent Act").

As the Petition explains, the obviousness requirement of 35 U.S.C. § 103 takes on heightened significance in the field of medicinal chemistry because a low threshold for nonobviousness "results in unchallengeable patents on marginal developments" to pharmaceutical drugs. Pet. at 20. This hinders rather than promotes the progress of science, *KSR*, 550 U.S. at 419, and harms consumers by foreclosing competition (and much lower prices) for prescription drugs, *see, e.g.*, *McNeil-PPC, Inc. v. L. Perrigo Co.*, 337 F.3d 1362, 1368 (Fed. Cir. 2003) ("[C]ompetition is foreclosed and the public is forced to pay higher prices."); *see also Schering-Plough Corp. v. FTC*, 402 F.3d 1056, 1065-66 (11th Cir. 2005) ("By their nature, patents create an environment of exclusion, and consequently, cripple competition."). In this particular case, the Federal Circuit's low threshold for nonobviousness is delaying market entry of generic equivalents to respondents' brand-name anti-hypertension drug Benicar.[3]

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3. As explained in the Petition, Benicar and the two combination products Benicar HCT and Azor are respondents' commercialized forms of olmesartan medoxomil, the compound covered by the '599 patent at issue. Olmesartan is an angiotensin II receptor blocker or ARB, as this type of compound is commonly known. *See* Pet. at 5.

The sheer magnitude of the prescription drug market highlights the importance of proper enforcement of Section 103's obviousness requirement. Total expenditures on prescription drugs approached a quarter of a trillion dollars in 2009. *See Expanding the Use of Generic Drugs*, APSE Issue Brief, U.S. Dep't of Health & Human Servs. (Dec. 1, 2010), at 6 ("*Expanding the Use of Generic Drugs*"), *available at* http://aspe.hhs.gov/sp/reports/2010/GenericDrugs/ib.pdf. This figure represents approximately 4 billion prescriptions, three-fourths of which were filled with generic equivalents of brand-name drugs. *See Savings Achieved Through the Use of Generic Pharmaceuticals, 2000-2009*, at 2 (July 2010) ("*Savings Achieved Through Generics*"), *available at* http://www.gphaonline.org/sites/default/files/GPhA%20Savings%20Study%20Book%20Updated%20Web%20FINAL%20Jul23%2010_0.pdf.

Generic prescription drugs save our national health care system a staggering amount of money. Indeed, "[f]or the decade 2000 through 2009, the use of generic prescription drugs in place of their brand-name counterparts saved the nation's health care system more than $824 billion dollars," and nearly $140 billion in 2009 alone. *Id.* at 1. For 2009, this "equates to a savings of . . . *more than $1 billion every three days.*" *Id.* at 2. Given the massive number of prescriptions nationwide, even a small increase in the utilization rate of generic drugs amounts to a huge cost savings. *See id.* at 5 ("[E]ach one percent increase in the nationwide generic utilization rate yields $4 billion in added savings . . . .").[4]

4. Generic drugs provide additional cost savings aside from their substitution for their brand-name counterparts. For example, they reduce the average branded price paid by consumers through the downward pressure on prices caused by competition. *See Expanding the Use of Generic Drugs* at 5.

Respondents' Benicar products, which are covered by the '599 patent, are anti-hypertension drugs. Hypertension is a serious health issue affecting nearly one-quarter of the world's population. "About 1 billion people suffer from hypertension, which accounts for about 7 million deaths per year," and "[t]he problem is rapidly worsening." *See* Margus Viigimaa, *ESH Hypertension Excellence Centres: A New Strategy to Combat an Old Foe*, J. Hypertension (2007), *available at* http://pt.wkhealth.com/pt/re/merck/pdfhandler.00004872-200708000-00037.pdf;jsessionid=Nn0VPZkrT9hTLJDcKsszFMZvNGy1yn9Jp5DjWhqm78JQyJTdFSg5!-1154299283!181195628!8091!-1. Since the introduction of respondents' Benicar products in 2002, these drugs have been prescribed over 58 million times and have accounted for over $4 billion in sales. *See Daiichi Sankyo Co. v. Mylan Pharm. Inc.*, 670 F. Supp. 2d 359, 384 (D.N.J. 2009). In fact, both "Benicar and Benicar HCT rank in the top 5% of U.S. prescription drugs in terms of sales." *Id.* This entire time, respondents' '599 patent has delayed entry by generic competitors, thus depriving the consumer public of lower prices and increased availability of anti-hypertension medicine for almost a decade. Indeed, those suffering from hypertension would benefit greatly from a lower-cost generic competitor, as data from the National Association of Chain Drug Stores indicates that "the average retail prescription price for a generic drug in 2009 was $39.73, 76 percent less than $155.45, the average cost for a branded drug." *Expanding the Use of Generic Drugs* at 5. And this benefit would be felt immediately. "Generic drugs can capture 80-90% of the market, often within months of entering the marketplace." Matthew Avery, *Continuing Abuse of the Hatch-Waxman Act by Pharmaceutical Patent Holders & the Failure of the 2003 Amendments*, 60 Hastings L.J. 171, 172 (2008).

Delaying the entry of generics to the market for prescription drugs causes real and substantial financial harm to the consumer public. For example, a Consumers Union study found that Medicare beneficiaries "taking five drugs [in common treatment areas] who switched from brand name drugs to lower-cost alternatives could save between $2,300 and $5,000 annually." *More Studies Find More Savings if Seniors Use Generic Drugs*, Senior J. (Mar. 3, 2006), *available at* http://seniorjournal.com/NEWS/MedicareDrugCards/6-03-03-MoreStudiesFind.htm. Rising costs of brand-name drugs will only exacerbate this financial harm. Indeed, "AARP determined that the average annual cost of prescriptions for a person taking three brand medicines *increased* $706 during the one-year period [ending March 2010], while the cost of generic versions of those same three medicines *decreased* by $51." *Savings Achieved Through Generics* at 5.

More importantly, delayed entry by generics is a public health hazard, particularly for those of limited means. Studies show that, in response to high costs for prescription drugs, "many seniors with serious health problems reported that they skip doses to make prescriptions last longer." 149 Cong. Rec. H7531, H7533 (2003). And a shockingly high number of Americans forgo needed prescription drugs altogether due to high costs. In 2008, the *Washington Post* reported on the results of a Rockefeller Foundation/Time Magazine survey that indicated that 23% of those surveyed declined to fill a medical prescription in the preceding year because of cost. *See* Ceci Connolly & Kendra Marr, *As Budgets Tighten, More People Decide Medical Care Can Wait*, Wash. Post, Oct. 16, 2008, *available at* http://www.washingtonpost.com/wp-dyn/content/article/2008/10/15/AR2008101503762.html?sid=ST2008101500125.

And because the federal government is the largest purchaser of prescription drugs, delayed entry by generics also harms the U.S. Treasury (and thus American taxpayers). The Centers for Medicare and Medicaid Services indicate that "in 2009 about 290 million prescriptions were purchased through the Medicaid program at a total cost of $23 billion," and that "generics enabled Medicaid to purchase 64% of these prescriptions (186 million) by using just $3.9 billion of the $23 billion spent for drugs." *Savings Achieved Through Generics* at 4.[5] But increased market entry by generics would produce significant additional savings, as "CMS data show that for every 2% increase in generic utilization, Medicaid saves an additional $1 billion annually." *Id.*; *see also Potential Federal & State-by-State Savings if Medicaid Pharmacy Programs were Optimally Managed*, The Lewin Group, at 1 (Dec. 2010), *available at* http://www.lewin.com/content/publications/Medicaid_Pharmacy_Savings_Report.pdf ("Medicaid FFS is less effective at encouraging the dispensing of generic drugs in place of brands. The generic dispensing rate in Medicaid FFS averages 68%, compared to an average 80% generic dispensing rate in Medicaid [managed care organizations].").

B. The Decision Below Sharply Conflicts With This Court's Decision In *KSR*.

KSR flatly rejected a "rigid approach" to obviousness, in favor of the "expansive and flexible approach" the Court has applied for decades. *KSR*, 550 U.S. at 415. This "functional" approach requires a "broad inquiry"

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5. *See also Expanding the Use of Generic Drugs* at 6 (noting that the CBO estimated that the availability of generic drugs for Medicare Part D "resulted in $33 billion in savings in 2007").

into the "interrelated teachings of multiple patents" and must "take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *Id.* at 415-18. This broad inquiry cannot fit within a "rigid and mandatory formula[]." *Id.* at 419. "Helpful insights" and "general principles" may provide guidance, but not when they are transformed into a "rigid rule that limits the obviousness inquiry . . . ." *Id.* at 419.

After instructing that a rigid framework was inappropriate, the *KSR* Court provided additional guidance for determining obviousness. The Court explained that focusing on particularized motivations for a patent claim is improper. *Id.* Rather, "[c]ommon sense teaches . . . that familiar items may have obvious uses beyond their primary purposes, and in many cases a person of ordinary skill will be able to fit the teachings of multiple patents together like pieces of a puzzle." *Id.* at 420. Further, the Court emphasized that a person of ordinary skill is "a person of ordinary creativity." *Id.* at 421. Thus, a patent claim may be proved obvious by a common-sense showing that the combination of elements was "obvious to try." *Id.* As the *KSR* Court cautioned, "[r]igid preventative rules that deny factfinders recourse to common sense are neither necessary under our case law nor consistent with it." *Id.*

The decision below applies the Federal Circuit's "lead compound" test, a test that is incompatible with *KSR* for at least two reasons. As an initial matter, the Federal Circuit utilizes the "lead compound" test as the *sole means* for determining obviousness. This narrowness is fundamentally at odds with *KSR*'s express rejection of a rigid, formulaic approach to obviousness.

Even setting aside this fundamental flaw, the "lead compound" test is still defective. Under the "lead compound" test, a patent challenger must demonstrate that a person having ordinary skill in the art of medicinal chemistry would have been motivated to select a lead compound and then would have been motivated to modify that compound in a manner that would result in the patented compound. *See Daiichi Sankyo Co.*, 619 F.3d at 1352. This test cannot be reconciled with how medicinal chemistry is actually practiced and conflicts with this Court's endorsement of the common-sense "obvious to try" inquiry. *See KSR*, 550 U.S. at 421 ("The . . . constricted analysis led the Court of Appeals to conclude, in error, that a patent claim cannot be proved obvious merely by showing that the combination of elements was obvious to try."). Certiorari is warranted so that the Court may review the decision below and provide the Federal Circuit with further guidance as to the appropriate standard for obviousness in the context of chemical compounds.

1. Employing the "Lead Compound" Test as the Sole Means of Assessing Obviousness is Incompatible with *KSR*'s Express Rejection of Rigid Tests.

The decision below errs from the start by employing a mechanistic two-step approach to determining obviousness. The test requires the patent challenger to show that a person having ordinary skill would have been specifically motivated to: (1) select a prior art compound as a lead compound, and (2) modify the lead compound to arrive at a claimed compound with a reasonable expectation that the new compound would have similar or improved properties compared with the old. *See Daiichi*

Sankyo Co., 619 F.3d at 1352; *see Takeda Chem. Indus., Ltd.*, 492 F.3d at 1357 ("[Even after *KSR*], it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness of a new claimed compound.").

Like the "teaching-suggestion-motivation" (TSM) test employed by the Federal Circuit before *KSR*, the "lead compound" test may be useful in analyzing obviousness. But, just like the TSM test, if the "lead compound" test is employed as the *sole means* of analysis, it "limits the obviousness inquiry," and thus is inconsistent with the *broad* obviousness inquiry of *KSR*. *See KSR*, 550 U.S. at 419 ("[W]hen a court transforms the general principle into a rigid rule that limits the obviousness inquiry . . . it errs."). There is no question that the decision below employs the "lead compound" test as the exclusive means for adjudging obviousness. *See Daiichi Sankyo Co.*, 619 F.3d at 1352.

Indeed, following *KSR*, many predicted that the Federal Circuit's "lead compound" test would not survive. *See, e.g.*, Scott D. Locke, *Protecting Pharmaceutical Inventions in a KSR World*, 50 IDEA 1, 12 (2009) (discussing "the tension between the CAFC and the Supreme Court in applying the obviousness standard when selecting a starting compound"); *Altana Pharma AG v. Teva Pharms. U.S.A., Inc.*, 532 F. Supp. 2d 666, 676 n.18 (D.N.J. 2007) (expressing doubt as to whether the lead compound requirement survived KSR), *aff'd*, 566 F.3d 999 (Fed. Cir. 2009). Yet, the Federal Circuit continues to use this rote formula. *See Daiichi Sankyo Co.*, 619 F.3d at 1354 (requiring "a motivation to select and then modify

a lead compound to arrive at the claimed invention"). Commentators thus have criticized the Federal Circuit for "significantly limit[ing] [*KSR*'s] impact on chemical compounds," in that "[t]he lead compound analysis is still the test for invalidating chemical patents." M. L. Hayes, *Three Years Post-KSR: A Practitioner's Guide to 'Winning' Arguments on Obviousness and a Look at What May Lay Ahead*, 9 Nw. J. Tech. & Intell. Prop. 243 (2010); *see also* Robert H. Resis, *Lessons to Learn: From Post-KSR Pharmaceutical Obviousness Decisions*, 2 Landslide 40, 40 (2009) (analyzing obviousness claims in the Federal Circuit since *KSR* and concluding that unless there are "persuasive reasons to start with a lead compound and then modify that lead compound to form the claimed drug, the claimed drug will be held to be nonobvious").

As a consequence, the Federal Circuit's undue confinement of the obviousness inquiry has effectively immunized chemical compound patents from obviousness challenges. The Federal Circuit has rejected *every* structural obviousness challenge to a patent claiming a new chemical compound since Congress passed the Hatch-Waxman Act in 1984. *See* Pet. at 3.

As the Petition explains, the "lead compound" test originally was not intended to be an exclusive test for obviousness in the chemical compound arena. Yet, as the result of an "unchecked propagation of error," this rigid test has become the sole method of determining obviousness for chemical compounds. *Id.* at 22-24; *see also* Vincent L. Capuano, *Obviousness of Chemical Compounds: the "Lead Compound" Concept*, Intellectual Property Today 33 (July 2007), *available at* http://www.iptoday

.com/pdf/2007/7/Capuano-July2007.pdf ("*Yamanouchi* has been mistaken as a new *per se* rule of obviousness in the chemical compound area. . . . In the proper context in which it arose, the 'lead compound' concept articulated in *Yamanouchi* is no more than a rejection of an argument made [in that case].") Thus, as in *KSR*, a grant of certiorari is warranted. *See KSR*, 550 U.S. at 419 ("[W]hen a court transforms the general principle into a rigid rule that limits the obviousness inquiry . . . it errs.").

2. The Rigid "Lead Compound" Test Conflicts With *KSR*'s Restoration of the Common-Sense "Obvious to Try" Inquiry.

As explained above, the "lead compound" test requires a patent challenger to demonstrate that a person having ordinary skill in the art of medicinal chemistry would have been motivated to select a lead compound and then would have been motivated to modify that compound in a manner that would result in the patented compound. *See Daiichi Sankyo Co.*, 619 F.3d at 1352; *Takeda Chem. Indus., Ltd.*, 492 F.3d at 1357. This unduly narrow test—which focuses on only one or a few so-called "lead" compounds—bears no relation to the practice of medicinal chemistry. It belies common sense and thus conflicts with the "obvious to try" inquiry this Court endorsed in *KSR*.

As a practical matter, the "lead compound" test makes no sense given the nature of medicinal chemistry. *See* Rebecca S. Eisenberg, *Pharma's Nonobvious Problem*, 12 Lewis & Clark L. Rev. 375, 377-78 (2008) ("In the chemical context, . . . often these inventions appear less obvious in hindsight than they seemed ex ante. Many standard modifications of prior art molecules are obvious

at least in the sense that a chemist of ordinary skill would be motivated to make them and would know how to make them . . . ."); *see also* Capuano, *supra*, at 33 ("A 'lead compound' requirement is inconsistent with the way new compounds are developed by chemists, and fails to reflect the realities and practices in the pharmaceutical industry.").

The practice of medicinal chemistry involves routine optimization through repeated trial and error: "A chemist, medicinal chemist, synthetic chemist, or anybody else in the business of making new organic compounds does so by routinely derivatizing and modifying previously known compounds." Capuano, *supra*, at 35. In doing so, a chemist of ordinary skill will select candidate compounds and attempt to modify those compounds in various ways in order to improve on the existing state of the art. *See id.* ("Known compounds having a desired activity are often considered for modification. Sometimes a group of compounds having a certain structural motif is described as having enhanced activity."). And although a medicinal chemist may identify certain lead compounds, that does not mean he will disregard all others. *Id.* ("Sometimes a single compound is selected as a lead compound for further study. Sometimes compounds are designated as 'back-up compounds' or otherwise considered valuable in the search for improved therapeutic molecules. A chemist considers all of these compounds having activity when designing new compounds, looking for structure-activity relationships and trends."). Thus, a test that requires the challenger to show that a medicinal chemist of ordinary skill would have been motivated to select a particular lead compound—or even a handful of lead compounds, *see Daiichi Sankyo Co.*, 619 F.3d at 1354 (affirming the

district court's decision to "select[] only five potential leads and . . . not includ[e] the '902 compounds among that finite number")—is incompatible with how the field of medicinal chemistry actually works.

The competition among pharmaceutical firms during the period at issue is instructive. As the Federal Circuit noted, "[f]ollowing losartan's success, over twenty different pharmaceutical companies, including Daiichi, established research programs to develop the next generation of ARBs." *Id.* at 1349. Notably, the patent applications submitted for new ARB compounds during this time each routinely disclosed dozens of related compounds. *See* Plaintiff's Trial Brief at 7-8, *Daiichi Sankyo Co. v. Mylan Pharm. Inc.*, Nos. 06-3462, 07-3039, 08-2752 (D.N.J. Dec. 22, 2008). This demonstrates that a narrow focus on only a few compounds does not square with the actual practice in this field.

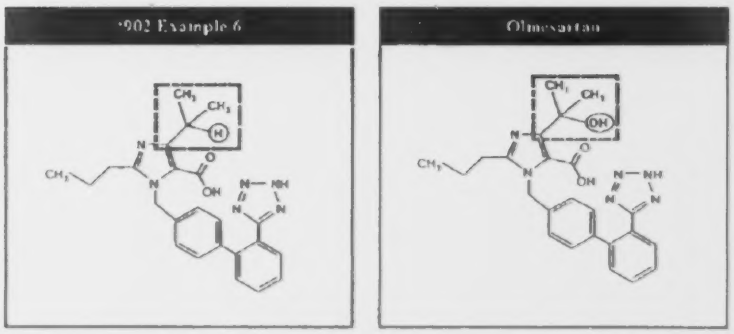
This massive disconnect between the inflexible "lead compound" test and the actual practice in the field indicates that the test is incompatible with the "obvious to try" inquiry. Indeed, the common-sense "obvious to try" inquiry is intended to reflect the actual practice in the relevant art. *KSR*, 550 U.S. at 421 ("When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.").

And a common-sense inquiry in this case would in fact have demonstrated the obviousness of the '599 patent. The following facts are undisputed:

- The '902 patent is structurally the closest prior art to Daiichi Sankyo's '599 patent. *See* Pet. App. 8a.

- The '902 compounds showed marked improvement over the previous generation of ARBs. *See* Pet. App. 74a.

- Olmesartan, the active ingredient in the patented compound, differs from one of the compounds disclosed by the '902 patent by a *single atom*. Olmesartan contains a hydroxyl group (–OH) at the 4-position of the imidazole ring; the '902 compound has a hydrogen atom (H) at that position. *See* Pet. at 7.



- A hydroxyl group is hydrophilic (or water-loving), and the prior art disclosed compounds with hydrophilic groups at the 4-position that had more favorable properties than the previous generation of angiotensin receptor blockers (ARBs). *See* Pet. App. 50a-51a.

- The 4-position was known to be the only feasible location where the compound could be modified.

See Br. of Appellants at 12-13, *Daiichi Sankyo*, 619 F.3d 1346 (filed Nov. 2. 2009) (discussing the testimony of Daiichi Sankyo's patentee, Dr. Yanagisawa).

- The only other modification Daiichi Sankyo made was the addition of a medoxomil group at the 5-position, but this was plainly obvious as medoxomil has been used by medicinal chemists to improve oral absorption of similar compounds for years. *See* Pet. at 7.

Given that medicinal chemistry involves an iterative trial-and-error process to modify known compounds in an effort to develop new compounds with more favorable properties than their predecessors, it would have been both routine and obvious for a person of ordinary skill to have modified the '902 compound by placing a hydroxyl group at the 4-position and adding a medoxomil group at the 5-position. In other words, it would have been obvious to create olmesartan and screen it for enhanced medicinal properties. But the "lead compound" test is far too narrow; it excludes consideration of (1) a compound disclosed by the closest prior art and that shows marked improvement over the previous generation of compounds in the relevant field; and (2) a slight modification shown to be an improvement over the previous generation of ARBs. Simply put, it is incompatible with the "flexible" and "functional" approach mandated by this Court and conflicts with the Court's endorsement of the "obvious to try" inquiry.

CONCLUSION

For the reasons set forth herein and in the Petition, amicus curiae GPhA respectfully requests that the Court grant the petition for a writ of certiorari.

Respectfully submitted,

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